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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/818,066	03/27/2001	Shuping Tong	00786-287004 / MGH-0960.3	1622
26161	7590	11/03/2004	EXAMINER	
FISH & RICHARDSON PC 225 FRANKLIN ST BOSTON, MA 02110			LUCAS, ZACHARIAH	
			ART UNIT	PAPER NUMBER
			1648	

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/818,066	<b>Applicant(s)</b> TONG ET AL.	
	<b>Examiner</b> Zachariah Lucas	<b>Art Unit</b> 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 10 August 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

1. Claims 1-9 are pending and under consideration. In the prior action, mailed on February 10, 2004, claims 1-9 were rejected. In the Response, filed on August 10, 2004, the Applicant amended claims 6.
2. Currently, claims 1-9 are pending and under consideration in the present application.

#### *Claim Rejections - 35 USC § 103*

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. **(Prior Rejection- Maintained)** Claims 1-5 were rejected under 35 U.S.C. 103(a) as being unpatentable over Khudyakov et al., J Virol 68: 7067-74 in view of the combined teachings of Chassot et al., Virology 200: 72-78 and Yuasa et al., Virology 181: 14-21. These claims read on polypeptides comprising a first part identical to residues 1-102, or fragments thereof comprising at least residues 80-102, of a hepadnavirus pre-S protein, and a second part comprising a sequence not identical to any part of the pre-S protein, and which may be glutathione S-transferase (GST). The Applicant traverses the rejection by arguing that the art cited provides no motivation for the combination of their teachings and that the claims are directed to non-obvious polypeptides "generated for specific purposes, e.g. to bind directly to

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receptor p120 and/or p120 to interfere with hepadnavirus infectivity,” and that. These arguments are not found persuasive.

The first argument in traversal is that no one of the cited references teaches or suggests the claimed peptides. While the Examiner agrees with this conclusion, it is not found to be a persuasive argument in that the rejection is based on the cumulative teachings of the references. This is because one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Because the rejection in this application is based on the cumulative teachings of the references, the Applicant’s arguments that no one of the them teaches the claimed peptides is not found persuasive.

The Applicant next argues that the cited art does not provide adequate motivation to combine the teachings of the references to make peptide according to the claimed invention. However, the art provides several examples of known antigenic epitopes within the region of amino acids 1-104 of the pre-S protein. In view of such, it would have been obvious to construct polypeptides comprising one or more of these epitopes. Further, as certain epitopes fall around the region of residues 80-102, it would also have been obvious to those in the art to make and use polypeptides comprising this region, and extensions thereof that comprise additional epitopes. Because the art discloses additional epitopes within the region (see e.g., Figure 22 of the application, and page 13 which states that these epitopes are found in the prior art), it would have been obvious to those in the art to make multiple epitope polypeptides of HBV which comprise this region of the pre-S protein. Thus, while the art does not specifically teach polypeptides

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consisting of residues 1-104 of a pre-S protein, or a fragment thereof comprising residues 80-102 of that polypeptide, such would have been obvious variants of the polypeptides suggested by the art, particularly in view of the teachings of Khudyakov which teaches the making and use of polypeptides comprising multiple epitopes of a target antigen.

The Applicant further argues that the claimed peptides have properties not disclosed in the prior art (the ability to bind to either p120 or p170). It is first noted that, at least with respect to the claims directed to fragments of the 1-104 peptide generally, there is no requirement in the claims that the peptides have this binding ability. Additionally, each of the claimed peptides comprises known neutralizing peptides, and from the teachings in the application (esp. Figures 9 and 21A), it would appear that any of the peptides of SEQ ID NO: 34 comprising the known epitopes would have this activity. See, Figures 9 and 21A (representing the peptides that can bind to one or both of p120 or p170), and Figure 22 (illustrating known peptides- see description of figure on page 13). The figures of the patent indicate that (a) each of the claimed peptides comprises at least 2 known epitopes, and that (b) each of the claimed peptides is able to bind one or the other targets (p120 or p170) for viral binding. Therefore, the peptides suggested by the prior art would, according to the Applicant's disclosure, bind one or the other of the target proteins. The Applicant is therefore asserting that the claimed peptides, i.e. any fragment of the 1-104 peptide, are patentable because they have properties which have gone previously unrecognized (the ability to bind either p120 or p170). However, as illustrated by section 2145 II of the MPEP, the mere recognition of previously latent properties does not render non-obvious an otherwise known invention.

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Applicant's assertion that the Office has used hindsight reasoning is noted, however, as the rejection is relying solely on information that was available to those in the art at the time the application is filed, this argument is not found persuasive. The Office nowhere relies on the teachings of the current application, or on the ability of the peptides to bind either p120 or p170, in the making of this rejection. This argument is therefore also found unpersuasive.

Because the prior art renders obvious the making of polypeptides comprising known epitopes of the HBV pre-S sequence, because each of the claimed peptides includes such known epitopes, and because the Applicant has distinguished the claimed peptides from those of the prior art merely by recognition of latent properties, the traversals of the rejection are not found persuasive. The rejection is therefore maintained for the reasons above, and the reasons of record.

5. **(Prior Rejection- Maintained)** Claims 6-9 were rejected under 35 U.S.C. 103(a) as being unpatentable over Khudyakov et al., J Virol 68: 7067-74 in view of the combined teachings of Chassot et al., Virology 200: 72-78 and Yuasa et al., Virology 181: 14-21. As noted by the Applicant, the claims have been such that they now require the polypeptide to include a fragment of the regions comprising residues 25-161 of the pre-S protein, and one or more sequences that are not identical to any part of the hepatitis B envelope protein. However, as Khudyakov teaches the use of polypeptides comprising multiple epitopes conjugated to a protein such as GST or B-galactosidase (see e.g. abstract) it is not clear what the relevance of this amendment is.

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While none of the cited references specifically teaches the claimed polypeptides, Khudyakov teaches the use of polypeptides comprising multiple epitopes of a target antigen, and each of Chassot and Yuasa teach that the pre-S protein comprise such epitopes. These later references additionally disclose epitopes that fall within the regions of the pre-S protein covered by the rejected claims. Because the art recognizes these regions as comprising known epitopes bound by anti-HBV antibodies, and because Khudyakov suggests the usefulness of polypeptides comprising such epitopes and fused to other non-viral (e.g. GST or  $\beta$ -galactosidase) sequences for the detection of antibodies, it would have been obvious to those in the art to construct polypeptides comprising these sequences. Although the art does not teach the specific regions claimed by the Applicant, the regions claimed are obvious in view of the teachings in the art with reference to the epitopes. While the Applicant has recognized latent properties of such polypeptides (the ability to bind to either p120 or p170), this does not render the claims non-obvious as was described above.

For the reasons above, and the reasons of record, the rejection is maintained.

### ***Conclusion***

6. No claims are allowed.
7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

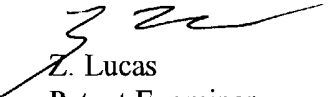
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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Z. Lucas  
Patent Examiner

  
JAMES HOUSEL 11/1/04  
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